

## REMARKS

Reconsideration and allowance are respectfully requested.

Claims 78-89, 91-94 and 98-104 are pending. The amendments are supported by the original disclosure and, thus, no new matter is added by their entry. Here, the “complex” is defined as associating the polymer and the substance by non-covalent bonds. Support for this definition can be found at page 10 of the present specification, where the term “complex” is defined as follows:

The term “complex” is used herein to denote an association between a . . . polymer . . . and another substance . . . the association between the components being primarily non-covalent, for example, involving any one or more of ionic, electrostatic and van der Waals forces. Although a complex according to the present invention predominantly involves non-covalent association between the components, there may nevertheless be some covalent bonding.

A complex is substantially different from a conjugate. In a complex, the bonding is non-covalent. In a conjugate, it is covalent. These compositions of matter have different properties. “Complex” is a term of art and a conjugate as cited below (i.e., Brocchini and Kuzuya) is not a complex, nor would it have been obvious to make the necessary modifications that chemically transform a conjugate into a complex. New claims 102-104, which are based on claims 92-94 and 99-101, depend from withdrawn claim 91.

Rejoinder of claims 94 and 101, which are drawn to methods of treatment using the elected complex, is requested upon allowance of the product claims. It is assumed that claims 91 and 102-104 would have to be pursued in a divisional application, but the Examiner’s confirmation of this assumption would be appreciated.

### *Statement of the Substance of the Interview*

The undersigned acknowledges the courtesy extended by the Examiner and his primary during the interview on June 13, 2011. The above amendment of claim 78 and the obviousness rejections were discussed. They agreed that this amendment would overcome the rejections of record, but that it would not be entered without a request for continued examination because amendment of claim 78 potentially raised new issues and required further search. The foregoing is Applicants’ summary of the interview. If anything else is required, do not hesitate to contact the undersigned.

*35 U.S.C. 103 – Nonobviousness*

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR Int'l v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* (“Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue”). Further, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 78-90, 92 and 98-99 were rejected under Section 103(a) as allegedly unpatentable over Brocchini et al. (WO 01/18080) in view of Kuzuya et al. (U.S. Patent 5,889,078) along with Junior et al. (WO 03/039435). Applicants traverse. A critical difference is that the present term “complex” as recited to describe the claimed invention and the term “conjugate” as understood in the art are distinct. One of ordinary skill in the art would not have found it obvious with a reasonable expectation of success to make the necessary modifications that chemically transform a conjugate into a complex.

Brocchini discloses a polymer with narrow molecular weight distribution used to produce polymer therapeutics and pharmaceutical preparations. But all polymer/drug conjugates disclosed by Brocchini contain polymer that is covalently bonded to drug. This can be seen very clearly in the reaction scheme on page 26 of WO 01/18080, which shows the preparation of doxorubicin conjugates. It is clear from Brocchini’s disclosure that only a covalently-bonded polymer/drug conjugate was envisaged: see for example, page 16, lines 9-11, “Conjugation of a bioactive agent or a derivative is carried out in a first reaction to covalently link the bioactive agent to the polymer”; page 19, line

4, "... may be covalently linked to a bioactive agent"; and page 19, lines 24-25, "The pendent chain Z may additionally be covalently bound to a ligand or bioactive agent."

Similarly, Kuzuya discloses a homopolymer of acrylic acid or methacrylic acid to which a physiologically active compound is covalently linked (see the general formula where  $R^2$  is the physiologically active compound). The disclosure of Junior et al. (WO 03/39435) is not relevant to using non-covalent bonds in a complex between polymer and drug or physiologically active compound.

In Applicants' claimed complex, the polymer and the substance having pharmacological activity against a pathogenic organism are associated by non-covalent bonds. But there is no evidence or reasoning presented in the Office Action that it would have been obvious for one of ordinary skill in the art to employ a complex associated by non-covalent bonds as required by Applicants' invention instead of a conjugate held together by covalent bonds as shown in the cited documents. Nor is there a reasonable expectation of success to do so. Instead, it is an essential feature of Brocchini and Kuzuya that the drug or the physiologically active compound is covalently linked to the polymer at each repeat unit.

If a modification proposed by the Examiner would change the principle of operation of the prior art invention being modified, then the cited prior art would fail to establish a prima facie case of obviousness. See *In re Ratti*, 123 USPQ 349 (CCPA 1959). Thus, the cited documents cannot be relied upon to establish a prima facie case of obviousness because their requiring covalent bonding between polymer and drug or physiologically active compound teaches against Applicants' claimed invention.

Therefore, the pending claims are patentable over Brocchini in view of Kuzuya along with Junior.

Claims 93 and 100 were rejected under Section 103(a) as allegedly unpatentable over Brocchini et al. (WO 01/18080) in view of Kuzuya et al. as applied to claims 78-90, 92 and 98-99, and further in view of Neely et al. (Eur. J. Clin. Microbiol. Infect. Dis. 19: 897-914, 2000). Applicants traverse because the terms "complex" and "conjugate" are distinct as explained above.

The disclosures of Brocchini and Kuzuya are discussed above. They disclose covalently-linked conjugates of polymer and drug only. Similarly, Neely's disclosure does not change the chemical nature of the bonds between polymer and drug. Applicants' claimed invention requires a complex between polymer and active substance associated by non-covalent bonds. Such is not disclosed in the cited documents.

Therefore, the pending claims are patentable over Brocchini in view of Kuzuya, and further in view of Neely.

Withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

#### *Double Patenting*

Claims 78-90, 92 and 98-99 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 3-6, 8, 11, 35 and 47-49 of Patent No. 6,803,438 in view of Kuzuya et al. (U.S. Patent 5,889,078). Applicants traverse because the '438 patent claims a conjugate having covalently-linked polymer and drug. No complex as required by Applicants' claimed invention is taught or made obvious by the '438 patent or Kuzuya.

Withdrawal of the double patenting rejection is requested.

#### *Conclusion*

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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